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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,555	08/29/2005	Erik Schwiebert	21085.0044U3	7032

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,555	SCHWIEBERT ET AL.	
	Examiner	Art Unit	
	JOHN PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,12,13,21-23,37,38,41-45,48-52,58,61,64 and 142-146* is/are pending in the application.

4a) Of the above claim(s) *37,38,41-45,48-52,58,61 and 64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,12,13,21-23 and 142-146* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-3, 12-13, 21-23, 37-38, 41-45, 48-52, 58, 61, 64, 142-146 are pending in this application.

Applicant's election with traverse of the invention of Group I, claims 1-3, 12-13, 21-23, and 142-146 (all in part as set forth in the previous Office action) in the response filed on 11/21/2007 is acknowledged.

Applicant's traversal is based on the erroneous argument that the serious burden requirement of a restriction requirement (MPEP 803) has not been met. Applicant is reminded that this application was filed under 35 USC 371, so MPEP 1893.03(d) applies:

> Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371.

Applicant does not traverse the lack of unity determination set forth in the previous Office action, so the propriety of said determination stands unrebutted.

Moreover, even though serious burden is not a required element of a proper lack of unity requirement, it is nonetheless met by the two inventions set forth in the previous Office action. Restriction for examination purposes is proper when the inventions are distinct (not disputed here) and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

See revised Form Paragraph 8.21 (May 2007).

Group I would require searching for ATP or ATP analogs, whereas Group II would require searching for ivermectin, which is not an ATP analog. At least reasons (c) and (d) would thus apply to raise serious burden.

Thus, even if applicant were not in error to argue serious burden, applicant's argument would fail because sufficient reasons have been given to establish serious and undue burden.

Pursuant to applicant's election, claims **1-3, 12-13, 21-23, and 142-146** will presently be examined *to the extent that they read on the elected subject matter*, and claims 37-38, 41-45, 48-52, 58, 61 and 64 are withdrawn from further consideration as being directed to non-elected subject matter.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 12-13, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Taylor et al., Schwiebert et al. (American Journal of Physiology, June 2001) and CAPLUS abstract 2001:30580.

Taylor et al. disclose that P2X purinergic receptor channels bind ATP and mediate Ca^{2+} influx and signals that stimulate secretory Cl^- transport across epithelia (abstract and Discussion section on pages 882-884). P2X receptors can be targeted to treat cystic fibrosis (p. 875, right column, last sentence of first paragraph).

Schwiebert et al. disclose that P2X receptors, on binding their ATP ligand, may increase cytosolic Ca^{2+} transiently and stimulate Cl^- and fluid secretion and ciliary beat frequency (Figure 2 on page F949). Purinergic agonists have been used to stimulate Cl^- and fluid secretions from cystic fibrosis tissues and epithelial cell models from the lung and airways and from the GI systems (page F957, last paragraph). In cystic fibrosis, Cl^- and fluid secretion are lacking but sodium absorption is augmented (id.). Purinergic agonist therapy is disclosed to potentially correct the abnormal handling of salt and water by the respiratory epithelium (p. F958, right column, first six lines; see also Figure 7).

CAPLUS abstract 2001:30580 is cited to establish that zinc ion is a known P2X receptor modulator that potentiates the actions of ATP in P2X receptor gated ion

channels.

Given the teachings of treating cystic fibrosis with P2X receptor agonists, the ordinary skilled artisan in this field would have been motivated to utilize the known agonist, zinc ion, to treat cystic fibrosis. Combined therapy with ATP is suggested from their coaction on the ion channels to bring about increased Cl^- transport and increased Ca^{2+}. Zinc chloride is suggested from its common availability as a zinc ion source. High calcium concentration is suggested from the known effect of calcium to activate epithelial chloride channels. In cystic fibrosis, sodium absorption is augmented, so lower sodium concentration in the treatment medium is suggested. Lower magnesium in the treatment is suggested in order to control one more variable in the complicated cascade of factors. The ordinary skilled artisan would have been motivated to deliver the treatment composition via conventional means to access the target cystic fibrosis diseased cells, e.g. via nasal spray, nebulizer or aerosol inhaler.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

Claims 1-3, 12-13, 21-23 and 142-146 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Taylor et al., Schwiebert et al. (American Journal of Physiology, June 2001), CAPLUS abstract 2001:30580 and Boucher, Jr. (US 6,926,911; hereinafter, Boucher) in view of Senior, Medline abstract

86146262 and Rubenstein et al. (US 2002/0115619).

Teachings of Taylor et al., Schwiebert et al. and CAPLUS abstract 2001:30580 have been discussed above, and the discussion there is incorporated herein by reference for clarity and to avoid repetition.

Boucher discloses treating cystic fibrosis patients with meglumine chloride, i.e. N-methyl D-glucamine chloride, via multiple delivery means and forms (column 3, lines 46 and 64 & see from column 5, line 26 to column 7, line 18). Combined use with other active agents to concurrently treat the patients is disclosed, including the use of ion transport modulator amiloride, which is a sodium channel blocker (column 7, line 20 to column 8, line 54; claims 1 and 5).

Senior discloses the role of pH in cystic fibrosis. Hyperacidification of golgi compartment in cells from cystic fibrosis patients may be related to increased bacterial adherence infections (first paragraph of the article; see also third column, first full paragraph). Medline abstract 86146262 discloses lower magnesium concentration to degrade exopolysaccharide produced by a bacterial strain of cystic fibrosis origin.

Disclosure by Rubenstein et al. is cited to further establish that cystic fibrosis is known to be treated with combination therapy wherein beneficial effects of multiple individual agents are combined (paragraphs 10-11).

Given the teachings of treating cystic fibrosis with P2X receptor agonists, the ordinary skilled artisan in this field would have been motivated to utilize the known agonist, zinc ion, to treat cystic fibrosis. Combined therapy with ATP is suggested from their coaction on the ion channels to bring about increased Cl^- transport and increased

Ca^{2+}. Zinc chloride is suggested from its common availability as a zinc ion source. High calcium concentration is suggested from the known effect of calcium to activate epithelial chloride channels. In cystic fibrosis, sodium absorption is augmented, so lower sodium concentration in the treatment medium is suggested. Lower magnesium in the treatment is suggested in order to control one more variable in the complicated cascade, and also to help combat bacterial exopolysaccharide that afflict cystic fibrosis cells. Alkalinizing extracellular fluid is suggested from the teaching that cystic fibrosis cells are hyperacidified, which could increase bacterial adherence. Amiloride and NMDG are suggested from the teaching that they are known therapeutic agents for cystic fibrosis. Combination of many different active agents to treat cystic fibrosis is suggested from its status as an incurable disease, which is known to be treated with combination of multiple agents. Additionally, the ordinary skilled artisan would have been motivated to deliver the treatment composition via conventional means to access the target cystic fibrosis diseased cells, e.g. via nasal spray, nebulizer or aerosol inhaler.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN PAK
PRIMARY EXAMINER